

### **REMARKS**

This Amendment accompanies a Request for Continuing Examination and is in response to the final Office Action dated August 15, 2005. Applicants filed a Response after Final and a Notice of Appeal on January 19, 2006. An Advisory Action issued January 30, 2006, indicated that the Response of January 19, 2006 was not entered. Applicants respectfully request continuing examination and present claim amendments and remarks in the present response. The claims, as presented in the last entered response dated July 8, 2005, are presented for amendment because the response dated January 19, 2006 was not entered. Also, the remarks presented below supersede those presented in the response of January 17, 2006.

By way of response, Applicants have amended claims 1-6, 8, and 19, cancelled claim 21, and added claims 25-31. Claims 1-6, 8-14, 16, 19-20, and 24-31 are pending. In light of the following remarks, Applicants respectfully request withdrawal of the pending rejections and advancement of this application to allowance.

#### **A. Amended and Added Claims**

Applicants have amended claims 1 and 19 to clarify that the HPLC column contains a solid support of superficially porous silica-based particles. These particles include alkylated and other derivatized forms of superficially porous silica-gel particles as described by the specification. This amendment is intended to further clarify the originally intended scope of the claims.

Applicants have further amended claims 1 and 19 to specify the amount of neutral, polar, fluorinated organic compounds, particularly 0.5 to 10%. The office action stated that neutral, polar, fluorinated organic compounds are not part of the claims because "less than 10%" reads on zero. This amendment is intended to clarify the originally intended scope of the claims includes neutral, polar, fluorinated organic compounds. Support for these amendments is found at least at page 16, lines 25-30.

Claim 19 is amended to reflect subject matter of original claim 21, while subject matter related to the mobile phase comprising an ion-pairing agent is now found in new dependent claims 25 and 28.

New claims 25 and 28 are supported throughout the specification including, for example, original claim 19 and page 19, line 26 through page 22, line 3.

New claims 26 and 29 are supported throughout the specification including, for example, page 25, lines 1-6; the Examples including temperature conditions at pages 36-39 and at page 4, line 21.

New claims 27 and 30 are supported throughout the specification including, for example, page 6, lines 8-9 and page 23, line 16 through page 24, line 19.

New claim 31 is supported throughout the specification including, for example, page 16, lines 29-30.

**B. Rejection of Claims Under § 103(a)**

Claims 1-6, 8-14, 16, and 19-24 stand rejected under 35 U.S.C. § 103(a) as obvious over Gilar (Analytical Biochemistry 298, 196-206 (2001)) (hereinafter "Gilar") in view of a Review of Waters' New Hybrid Particle Technology and Its Use in High Performance Liquid Chromatography (HPLC), pages 1-4 (1999) (hereinafter "Waters"). Applicants respectfully traverse these rejections and do not concede any characterizations of the claims or the cited references made in the office action.

**1. Cited Art Does Not Disclose Superficially Porous Silica-based reversed-phase support**

In support of the rejection, the office action states it is obvious that Gilar's "Xterra MS C18 is a "silica based" support because Waters evidences that Gilar discloses a silica based support. Applicants disagree.

Waters in combination with Gilar does not teach "silica-based" supports as set forth in the pending claims and defined in the specification. The superficially porous silica-based reversed-phase support of the pending claims refers to a support composed of particles comprising a solid core and macroporous shell of silica. See, for example, page 23, lines 7-10, "The inventive HPLC methods may be carried out using any suitable silica gel-based reversed-phase stationary support composed of superficially porous particles (i.e., microparticulate silica having a solid core and a thin porous shell)." The solid core and macroporous shell of **silica** may be further derivatized on the surface as described on pages 23-24 of the specification. Hence, the particles are described as "silica-based."

In contrast, Waters teaches (and Gilar makes use of) a hybrid particle that "is a member of a class of material known as organic/inorganic hybrids. Water's hybrid particles

contain inorganic (e.g. silica) and organic (e.g. organosiloxane) elements, and thus share the advantages of both." See Waters at pages 1-2. Water's fully porous particles formed from a mixture of silica units and organosiloxane units are substantially different and have substantially different properties from the silica-based particles of the present application. Indeed, Waters distinguishes itself from silica-based particles in teaching, "There is no way to meet such demands simply by modifying existing processes while maintaining the underlying silica base materials. The goal with hybrid technology was to take a quantum leap to a higher level of performance by radically changing the composition of the underlying chromatographic particle itself." Page 1 (emphasis added). The reference then goes on to explain the properties of the hybrid chromatographic particle and how they are different than silica-based particles (see, e.g., Figures 2-5).

The Waters' support represents a different solution to the problem of silica particle degradation in HPLC supports. Waters developed a new particle having an altered chemical composition that is more resistant to degradation. In contrast, the claimed method for extending column life is applicable to existing superficially porous silica-based supports without reengineering the solid support.

It is also important to note that Waters' does not teach a superficially porous support as set forth in the pending claims and defined in the specification. A superficially porous stationary support is defined at page 9, lines 19-21 as a solid support composed of particles having a solid core and a thin porous shell. In contrast, Waters' hybrid is a fully porous particle.

Therefore, Waters does not support the proposition that Gilar discloses a silica based support for the Xterra MS C18 or a superficially porous silica-based supports as set forth in the pending claims.

## **2. Gilar Fails to Teach "An Increased Column Lifetime"**

Claim 1 (and hence dependent claims 2-6, 8-14, 16) sets forth the presence of the neutral, polar, fluorinated organic compound in the mobile phase leads to an increased column lifetime. In sharp contrast, Gilar teaches choosing materials for an HPLC that increase the efficiency of separation and thus enhances mass spectrometry detection because they do not interfere with ionization within the mass spectrometer. There is no teaching or suggestion for including a stabilizer of the stationary phase in the mobile phase composition.

Waters also fails to disclose that the presence of the neutral, polar, fluorinated organic compound in the mobile phase leads to an increased column lifetime. Furthermore, Gilar and Waters, either alone or in combination, do not teach that 0.5 to 10% by volume of a neutral, polar, fluorinated organic compound should be included in an aqueous mobile phase. In particular, neither Gilar nor Waters teach that 0.5% to 2% of a polyfluorinated alcohol in an aqueous mobile phase will extend the column lifetime of a superficially porous, silica based HPLC support as required in claim 31.

Therefore, no combination of the cited references sets for all of the claimed elements set forth in claim 1 and its dependent claims (claims 2-6, 8-14, and 16).

### **3. Waters Explicitly Teaches Away From the Claimed Invention**

Waters explicitly teaches away from using a superficially porous silica based reversed-phase support. For example, Waters states, "There is no way to meet such demands simply by modifying existing processes while maintaining the underlying silica base materials. The goal with hybrid technology was to take a quantum leap to a higher level of performance by radically changing the composition of the underlying chromatographic particle itself." Page 1 (emphasis added). This passage from waters explicitly teaches away from using superficially porous substantially pure inorganic silica particles do not work and that one must use hybrid particles instead.

Therefore, one would not consider the Waters' reference or a combination that includes the Water's reference to achieve the claimed invention. The applicants respectfully submit that the claims are patentably distinct from the cited references and request withdrawal of the pending rejection.

### **Summary**

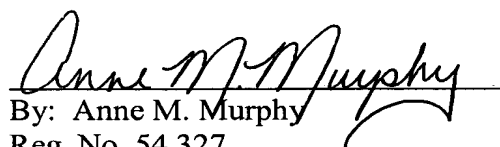
In view of the foregoing remarks, Applicants respectfully submit that all of the pending claims are patentably distinct over the cited reference and request withdrawal of the pending rejections. Applicants further request advancement of this application to allowance.

Applicants note that there may be reasons that the pending claims are patentably distinct in addition to those raised in this response. Applicants reserve the right to raise any such argument in the future.

The Examiner is encouraged to contact the undersigned attorney at the telephone number shown below with any questions and/or in effort to expedite prosecution of this application.

Respectfully submitted,  
MERCHANT & GOULD P.C.  
P.O. Box 2903  
Minneapolis, Minnesota 55402-0903  
(612) 332-5300

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By: Anne M. Murphy  
Reg. No. 54,327  
AMM:pll